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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/988,792	11/20/2001	Andrzej W. Lipkowski	18475-025 (NEMC-6)	9119

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EXAMINER	
FORD, VANESSA L	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 01/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/988,792	LIPKOWSKI ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *October 16, 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-24,31-43 and 47-54* is/are pending in the application.

4a) Of the above claim(s) *15-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-43 and 47-54* _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

FINAL ACTION

1. This Office Action is responsive to Applicant's amendment and response filed October 16, 2003. Claims 1-14, 25-30 and 44-46 have been cancelled. Claims 47-54 have been added.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Rejections Withdrawn

3. In view of Applicant's amendment and response the following rejections are withdrawn:

a) Rejection of claims 1, 8 and 31-39 under 35 U.S.C. 112, first paragraph, pages 2-5 of previous Office action.

b) Rejection of claims 1-3, 7, 1-13, 24-27, 29-30 and 44-46 under 35 U.S.C. 102(b), pages 8-9 , paragraph 5 of previous Office action.

c) Rejection of claims 1,3, 7-8, 10-13, 24-27, 29-30 and 44-46 under 35 U.S.C. 102(b), pages 10-11, paragraph of previous Office action.

d) Rejection of claims 1-3, 7-8, 10-13, 24-27, 29-30 and 44-46 under 35 U.S.C. 102(b), pages 13-14, paragraph 8 of previous Office action.

e) Rejection of claim 24 under 35 U.S.C. 112, second paragraph, page 14, paragraph 9 of previous Office action.

f) Rejection of claim 25 under 35 U.S.C. 112, second paragraph, pages 14-15, paragraph 10 of previous Office action.

g) Rejection of claims 29 and 30 under 35 U.S.C. 112, second paragraph, page 15, paragraph 11 of previous Office action.

h) Rejection of claims 32-39 under 35 U.S.C. 112, second paragraph, page 15, paragraph 12 of previous Office action.

i) Rejection of claim 45 under 35 U.S.C. 112, second paragraph, page 15, paragraph 13 of previous Office action.

j) Rejection of claim 46 under 35 U.S.C. 112, second paragraph, pages 15-16, paragraph 14 of previous Office action.

k) Rejection of claims 1-2, 7, 11, 14, 24, 26, 28-34, 36, 38 and 40-46 under 35 U.S.C. 102(b), pages 16-17 , paragraph 15 of previous Office action.

Rejections Maintained

4. The rejection of claims 31-43 and newly submitted claims 47-54 under 35 U.S.C. 112 first paragraph is maintained for the reasons set forth on pages 5-8, paragraph 4 of the previous Office Action.

The rejection was on the grounds that the claims were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID Nos: 1 and 2 does not reasonably provide enablement for the full breadth of the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification is enabling only for the polypeptides of SEQ ID NOs: 1 and 2 as disclosed in the specification. The specification states that "Substance P peptides are at least 50% identical to the sequences of SEQ ID No: 1 or 2." The specification also teaches that the substance P peptides art at least 75%, 85%, 95% and 99% identical to the SEQ ID Nos. 1 or 2". The specification further states that " a conservative substitution of one amino acid for another is a replacement by an amino acid having similar chemical functional side group, e.g. replacement by another amino acid by another positively charged amino acid or replacement of a hydrophobic amino acid by another hydrophobic amino acid" (page 7). There is no guidance provided as to which amino acids can be added, deleted or substituted and the polypeptide would retain its biological function. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Since the amino acid sequence of the polypeptide determines its structural and functional properties, predictability of which changes can

be tolerated in a polypeptide's amino acid sequence and still retain similar activity requires a knowledge with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expected intolerant to modification) and detailed knowledge of the ways in which the polypeptide's structure relates to function. However, the problem of the prediction of polypeptide structure from mere sequence data of a single polypeptide and in turn utilizing predicted structural determinations to ascertain functional aspects of the polypeptide and finally what changes can be tolerated with respect thereto is extremely complex and outside of the realm of routine experimentation.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen multiple substitutions or multiple modifications of other types and the positions within the polypeptide's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity are limited in any polypeptide and the result of such modifications is unpredictable based on the instant disclosure. One skilled in the art would expect any tolerance to modifications, e.g., multiple substitutions. The sequence of some polypeptides is highly conserved and one skilled in the art would not expect tolerance to any amino acid modification in such polypeptides.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to selecting other antigens having claimed functional features, 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). One of skill in the art would require guidance, in order to make or use polypeptides that are variants of SEQ ID NOs: 1,2 and SEQ ID Nos: 12 and 13 in a manner reasonable in correlation with the scope of the claims. Without proper guidance, the experimentation to make and use these polypeptides is undue.

Applicant urges that the claims are fully enabled. Applicant urges that claims 1 and 8 have been cancelled and claims 31-39 were amended to require residues 1-8 of SEQ ID NO:1 or SEQ ID NO:2 and to require that 1, 2 or all 3 carboxy-terminal amino acids of the corresponding sequence are not present. Applicant urges that the

specification teaches that antimicrobial activity of an SP peptide is unrelated to SP receptor bind and that SP receptor binding involves the carboxy-terminal end of SP. Applicant also urges that the carboxy-terminal 1, 2, or 3 amino acids of SP are not required for antimicrobial activity. Applicant urges that the claims have been amended to show exactly which amino acids are required to retain biological function, (i.e. antimicrobial activity).

Applicant's arguments filed October 16, 2003 have been fully considered but they are not persuasive. The claims are drawn to a composition comprising a fragment of a substance P peptide wherein said fragment comprises antimicrobial activity and does not bind to a cell surface substance P peptide receptor and wherein said fragment comprise residues 1-8 and does not comprise residues 9, 10 or 11 of SEQ ID NO: 1. The claimed invention also encompasses compositions comprising amino acids 1-9 and 1-10 of SEQ ID Nos: 1 and 2, which do not bind to a cell surface substance P peptide receptor. As disclosed above in Applicant's arguments, the specification teaches that antimicrobial activity of a SP peptide is unrelated to SP receptor binding, that SP receptor binding involves the carboxy-terminal end of SP and that the carboxy-terminal 1, 2, or 3 amino acids of SP are not required for antimicrobial activity. However, the specification also teaches that the SP peptides of the invention associate with a membrane component of a microbe and do not associate with a SP receptor, for example the tachykinin receptor (page 2). The specification teaches that the SP receptor involves the carboxy-terminal end of SP (page 7). The specification teaches that the three carboxy or C terminal amino acids (i.e. amino acids 9, 10 and 11 of SEQ

ID Nos: 1 and 2) confer on SP the ability to interact with a specific SP receptor on immune cells (page 12). The specification teaches that the 8-residue fragment of SP has antimicrobial activity but does not bind to a SP receptor since the fragment lacks the portion of the peptide that confers affinity to the receptor (page 12). The specification is enabled for this peptide fragment. Would the peptides that comprise amino acids 1-9 and 1-10 of SEQ ID Nos: 1 and 2 possess some binding properties? One of skill in the art would not conclude that the claimed compositions comprising amino acids 1-9 or amino acid 1-10 of SEQ ID Nos 1 or 2 would not possess SP receptor binding properties since the carboxy-terminal amino acids 9, 10 and 11 of SEQ ID NO: 1 and 2 are required to confer on SP the ability to bind to immune cells. The specification fails to provide this information. Therefore, the instant specification is not enabled for a composition comprising a fragment of the substance P peptide that comprises amino acids 1-9 or 1-10 of SEQ ID Nos: 1 or 2 and does not bind a cell surface substance P receptor.

5. The rejection under 35 U.S.C. 102(b) is maintained for newly amended claims 31-39 and newly submitted claim 47 and 52-53 for the reasons set forth on pages 7-8 paragraph 7 of the previous Office Action.

The rejection was on the grounds that De Simone et al teach the effects of substance P on *Salmonella minnesota*. De Simone et al teach that substance P inhibits the binding of blood lymphocytes and bound-bacteria/lymphocytes. De Simone et al teach that substance is able to hamper the bacterial cytoadherence to T cells. De Simone et al discloses that substance P is involved in the mechanism of host protection against invading microorganisms (see the abstract). The recitation of an "antimicrobial composition" is being viewed as a limitation of intended use. The amino acid sequences of substance P would be inherent in the teaching of the prior art.

Since the Office does not have the facilities for examining and comparing applicant's composition with the composition of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the composition of the prior art does not possess the same material structural and functional characteristics of the claimed composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

It should be noted that Applicant did not address this rejection.

New Grounds of Rejection Necessitated by Amendment

Claim Objections

6. Claim 35 is objected to for the following informalities: line 2 of the claim recites "1-8 2". The "2" should be deleted. Correction is required.

7. Claims 40-43 depend from a cancelled claim. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 32 and 33 are rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 32 and 33 fail to further limit claim 31. Clarification is required.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
January 21, 2004

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